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chain nodes :
   7 8 16 17 23
                    24
                        36
                           37
                               38
                                   39
                                          47
ring nodes :
   1 2 3 4 5 6 10
                        11
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                                  14
                                      15
                                          25 26
                                                 27 28
                                                        29 30 31 32 33 34 35
ring/chain nodes :
   9
chain bonds :
   2-47 3-23 4-7 8-9 16-17 26-31 36-37 37-38 37-39
ring bonds :
   1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15 25-26 25-29
   26-27 27-28 28-29 30-31 30-35 31-32 32-33 33-34 34-35
exact/norm bonds :
   1-2 1-6 2-3 2-47 3-4 3-23 4-5 4-7 5-6 8-9 10-11 10-15 11-12 12-13 13-14
   14-15 16-17 25-26 25-29 26-27 27-28 28-29
exact bonds :
   26-31 36-37 37-38
                      37-39
normalized bonds :
   30-31 30-35 31-32 32-33 33-34 34-35
G1: [*1], [*2], [*3]
G2: [*4], [*5], [*6], [*7]
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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom

35:Atom 36:CLASS 37:CLASS 38:Atom 39:Atom 40:Atom 47:CLASS

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:Atom 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom

Match level :

17:

Generic attributes :

10/802,765 Page 1

=> d his

(FILE 'HOME' ENTERED AT 12:07:18 ON 14 APR 2005)

FILE 'REGISTRY' ENTERED AT 12:07:30 ON 14 APR 2005

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 8 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:08:11 ON 14 APR 2005

L4 15 S L3

=> d que 14 stat

L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

L3 8 SEA FILE=REGISTRY SSS FUL L1

L4 15 SEA FILE=CAPLUS ABB=ON PLU=ON L3

=> d 1-15 bib abs hitstr

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ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 2003:76766 CAPLUS 138:131144
 AN
DN
TI
IN
PA
SO
       138:131144
Aryl-substituted thiazolidinones and therapeutic use thereof
Sun, Qun; Kyle, Donald J.
Euro-Celtique, S.A., Duxembourg
PCT Int. Appl., 45 pp.
CODEN: PIXXD2
 DT Patent
LA English
FAN.CNT 1
PATENT NO.
KIND DATE
                                                            APPLICATION NO.
                                                                                            DATE
        MARPAT 138:131144
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The invention discloses aryl-substituted thiszolidinones I $\{n=1,\ 2\}$ R1 - YN(R3)(R4) (Y = alkylene; R3, R4 = H, alkyl, aryl, or R3 and R4 together form alkylene chain having 4-5 C optionally interrupted by N or O), pyridylalkyl, optionally substituted pientidin-4-yl; R2 - optionally substituted phenoxyphenyl, optionally substituted phenylchiophenyl, optionally substituted benzyloxyphenyl, etc.), or a pharmaceutically acceptable salt or solvate thereof. The invention also discloses the use of I for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions, e.g. amyotrophic lateral sclerosis, and for the treatment, prevention or

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ANSWER 2 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 2001:428220 CAPLUS 135:272658
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Intramolecular C-H--O interaction between lactam oxygen and N-alkyl

CS 50

PB DT LA AB

list:272658
Intramolecular C-H--O interaction between lactam oxygen and N-alkyl protons
Barone, V., Bolognese, A., Correale, G., Diurno, M. V., Gomez-Monterrey, I., Mazzoni, O.
Dipartimento di Chimica, Universita di Napoli "Federico II", Naples, Italy Journal of Molecular Graphics & Modelling (2001), 19(3/4), 318-324
CODEN: JMGHFI, ISSN: 1093-3263
Elsevier Science Inc.
Journal
English
We report evidence of an unusual C-H--O interaction between an a-methylene hydrogen of the alkylamine chain of substituted (N,N-dimethylamino)propyl-thizaridinones and substituted (N,N-dimethylamino)propyl-thizaridinones and substituted (N,N-dimethylamino)propyl-thizaridinones and substituted (N,N-dimethylamino)propyl-thizaridnessing substituted (N,N-dimethylamino)propyl-thizaridnessing substituted (N,N-dimethylamino)propyl-thizaridnessing substituted (N,N-dimethylamino)propyl-thizaridnessing substituted (N,N-dimethylamino)propyl-thizaridnessing catchylaminos and the lactam carbonyl oxygen. NMR anal. results, supported by mol. mechanic protoctions, were in agreement with ab initio calchs. The observed interaction shortening the nitrogen-nitrogen distance in the HI-histamine antagonist, 2-(4-methylphenyl)-3-(3-(N,N-dimethylamino)propyl-1,3-thizaclidin-4-one, could explain its fitting with the HI-antihistaminic pharmacophoric model and the high antihistaminic activity.

JS3602-74-89
KL: PRP (Properties), SPN (Synthetic preparation), PREP (Preparation)

RI: PRP (Properties); SPN (Synthetic preparation); PREF (Preparation) (intramol. C-H--O interaction between lactam oxygen and N-alkyl protons)

protons)
363602-74-8 CAPLUS
4H-1,3-Thiazin-4-one, 3-{3-(dimethylamino)propyl}tetrahydro-2-{4-methylphenyl}- (9CI) (CA INDEX NAME)

(CH₂) 3-NMe₂

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT RE.CNT 27

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
amelioration of both acute and chronic pain, of depression, as local
anesthetics, as antiarrhythmics and for the treatment or prevention of
diabetic neuropathy. The compds. of the invention are sodium channel
blockers.

17 491864-53-0 491864-87-0

491864-53-0 491864-97-0
RI: FAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aryl-substituted thiazolidinones and therapeutic use)
491864-53-0 CAPUS
4H-1,3-Thiazin-4-one, 2-(2,2-diphenylethenyl)tetrahydro-3-[2-(1-piperidinyl)ethyl)- (SCI) (CA INDEX NAME)

491864-87-0 CAPLUS
4H-1,3-Thiazin-4-one, 3-[2-(dimethylamino)ethyl]-2-(2,2-diphenylethenyl)tetrahydro- (9CI) (CA INDEX NAME)

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 2000:819473 CAPLUS 134:5159

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	US	5807	829			A		1998	0915		US	1996	-7611 -2272	90		1	9961	206
	CA	2272	548			AA		1998	0611		CA	1997	-2272	548		1	9971	205
	WO	9824	806			A2		1998	0611		WO	1997	-US21	636		1	9971	205
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			PL,	PT,	RO,	RU,	SD,	SE,	SG,	51,	SK	, sL	, TJ,	TM.	TR.	TT.	UA.	UG
			UΖ,	VN,	YU,	ZW,	AM,	AZ,	BY.	KG.	KZ	. MD	. RU.	TJ.	TM			
		RW:	GH,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	AT	, BE	, сн,	DE.	DK.	ES.	FI.	FR.
			GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE	, BF	, BJ,	CF,	CG,	CI,	CM.	GΑ,
			GN,	ML,	MR,	NE,	SN,	TD,	TG									
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	ΕP	9545	26			A2							-9522			15	9971	205
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				SI,			FI,											
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	RU	2217	436			CZ		2003			RU	1999	-1146	06			9971	
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ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Tripeptides I [X, Y = O, N, or S, provided that at least one of X or Y = N; Ri = (un) substituted (C5-12) aryl, (C5-12) arylalkyl, (C5-12) arylalkenyl, fused (C5-12) aryl-cycloalkyl, alkyl- or alkenyl-fused (C5-12) aryl-cycloalkyl, alkyl- or alkenyl-fused (C5-12) aryl-cycloalkyl optionally comprising one or more heteroatoms selected from N, S, or non-peroxide O; R2, R3 = H or alkyl; A = CO, NHCO, SO2, OZC, Or CHZ; R4 = H, alkyl, alkenyl, cycloalkyl, aryl, or arylalkyl (with provisos)] were prepared as serine protease inhibitors, including inhibitors of human neutrophil elastase. Thus, peptide I (Cbz = benzyloxycarbonyl) (CE-2072) was prepared and showed Ki = 0.025 nM for inhibition of elastase.

208845-99-4P, Ce-2119

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of tripeptoid analogs as serine protease inhibitors)

208845-59-4 CAPLUS

2H-1,3-Thiazine-3(4H) -acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methyl)penyl)-al-methyl)-1,3,4-oxadiazol-2-yl)carbonyl]propyl-4-oxo-2-phenyl-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
2000:47017 CAPLUS
132:78559
Preparation of heterocyclic compounds as serine protease inhibitors
Gyorkos, Albert; Spruce, Lyle W.
Cottech Inc., USA
U.S., 107 pp., Cont.-in-part of U.S. 5,891,852.
CODEN: USXKAM
Patent
English
N.CRT 18
PATENT NO. KIND DATE APPLICATION NO. DATE DT LA FAN APPLICATION NO.

US 1997-984881
US 1994-345820
US 1996-762381
CA 1997-2272548
WO 1997-US21636

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

The present invention relates to a series of compds. of general structure I (X, Y = 0, N, or S provided that at least one of X or Y = N, R1 = CS-12 arylalkyl, or CS-12 arylalkyl with at least one N, S, and Or R2, R3 = H or alkyl, B = S(0)2 or C(0), R6 = heterocycles (generic structures given)) that are useful as serine protease inhibitors, including inhibitors for human neutrophil elastase. In an in vitro test for inhibition of elastase, the title compound II shows the KI value of 78.3. Compds. of the invention are useful in treating conditions such as adult respiratory distress syndrome, septic shock, and multiple organ failure. failure. 208845-59-4P

IT RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of heterocyclic compds. as serine protease inhibitors)

BIOL (Biological study); PREF (Preparation), Value (Note), (preparation of heterocyclic compds. as serine protease inhibitors) 208845-59-4 CAPIUS 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 1999:794318 CAPLUS 132:23197 Preparation of N-substituted prolinyl peptide analogs as serine protease inhibitors Gyorkos, Albert; Spruce, Lyle W. Cortech Inc., USA U.S., 107 pp., Cont.-in-part of U.S. 5,869,455. CODEN: USXXXAM PALEAT
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V: AL, AM, AT, AU, AZ, RA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JF, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, HD, HG, HK, HM, HM, HX, ND, NZ, FL, FT, RD, NW, SD, SE, SS, SI, SK, SL, JJ, HT, RI, TI, AU, UG, UZ, VM, YU, ZW, AM, AZ, BY, KG, KZ, HD, RU, TJ, TM, CB, GR, IE, IT, LU, HC, NL, FT, SE, BF, BJ, CF, CG, CI, CM, GA, MI, MR, ES, NT, DT, TG

AU 9858894

Al 19880629

AU 1998-55894

AU 1998-55894

AU 1998-55894

BE 20010621

EP 954526

AZ 19991110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT.
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                                      2010621 B2 2010621 BP 1997-95232 19971205

8: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, LE, SI, LT, LV, FI, RO
1247542 A 20000315 CN 1997-180392 19971205

9901661 12 20000321 TR 1999-9901661 19971205
2001507679 T2 20010612 JP 1999-525656 19971205
220169 B2 20011022
200103270 T2 20030321 TR 2001-200103270 19971205
22017436 C2 20031127 RU 1999-11606 19971205
2217436 C2 20031127 RU 1999-11606 19971205
2037325 A 20000314 US 1998-69923 19980430
9902734 A 19990802 NO 1999-2734 19990604
1994-345820 A 20000531 MX 1999-5240 19990604
1994-345820 A 219941121
1996-761313 A2 19961206
                       CN 1247542
TR 9901681
JP 2001507679
JP 3220169
TR 200103270
RU 2217436
WX 9905240
US 1994-345820
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US 1996-761313
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US 1996-761310
US 1997-985201
US 1997-985056
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MARPAT 132:23197
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132:36032
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Preparation of prolinyl peptide analogs as serine protease inhibitors Gyorkos, Albert; Spruce, Lyle W. Cortech Inc., USA, U.S., 110 pp., Cont.-in-part of U.S. 5,801,148.
CODEN: USXXMM
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ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 1999:779215 CAPLUS

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN

$$R^{14}-A-D-NR^{10}CH_2CONHCR^2R^3CO$$
 $N=X$
 R^1
 R^1

Proline analogs I [X, Y = 0, S, N or substituted N, Rl = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloslkyl, alkenylcycloslkyl, slkenylcycloslkyl, cycloslkenyl, alkylcycloslkenyl, alkenylcycloslkenyl, aryl, arylalkyl, arylalkenyl, alkylcycloslkenyl, alkenylcycloslkenyl, arylalkyl, arylalkenyl, art., R2, R3 = H, (un)substituted alkyl or alkenyl, arylalkyl, arylalkenyl, arylalkyl, arylalkyl, cycloslkyl, aryl, cycloslkyl, etc., R10 = aryl, arylalkyl, alkylalkenyl, cycloslkyl, aryl, cycloslkyl, etc., R10 = aryl, arylalkyl, arylalkenyl, cycloslkyl, alkylcycloslkyl, etc., D is a direct bond or an amino acid selected from proline, isoleucine, cyclohexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, MHCO, SOZ, COC, CHIZ, R14 = H, alkyl, alkenyl, aryl, arylalkyl, cycloslkyl, alkylcycloslkyl, etc., were prepared as serine protease inhibitors. Thus, (benzylosycathonyl)-1-valyl-N-[16]-[5-[3-methylbenzyl]-1,3,5-oxadiazolyl]carbonyl]-2-methylpropyl]-1-prolinamide was prepared and showed K1 = 0.025 nM for inhibition of human neutrophil elastase.

208845-59-4P, CE 2118

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, nolassified); SFN (Synthetic preparation); TRU (Therapeutic use); BIO. (Biological study); PREP (Preparation); USES (Uses)

(preparation of prolinyl peptide analogs as serine protease inhibitors)

208845-59-4 CAPLUS

ZH-1,3-Thiazine-3 (4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[(5-[(3-methyl-1henyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-obute stereochemistry.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

Proline analogs I (X, Y = 0, S, N or substituted N; Rl = (un)substituted alkyl, alkenyl, or alkynyl, hydroxy, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkyl, cycloalkenyl, alkylcycloalkyl, alkenylcycloalkyl, cycloalkyl, erylalkenyl, etc.; R2, R3 = H, (un)substituted alkyl or alkenyl, -RCOR', -RCOZR', -RROR'R'RO, or -RCORN'R'', where R is alkyl or alkenyl and R', R'', and RO are H, alkyl, alkenyl, cycloalkyl, aryl, cycloalkyl, etc.; B = SOZ, CO, CC, CHZCOZ R6 = aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, or R14-A-D-NRYCHRS-, where RYRB is o-(CH2)nCGH4(CH2)n (m, n = 0, 1), D is a direct bond or an amino acid selected from proline, isoleucine, cyclobexylalanine, or cysteine optionally substituted at sulfur, A is a direct bond, CO, NHCO, SOZ, OCO, CH2; R14 = H, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, alkylcycloalkyl, etc.) were prepared as serine protease inhibitors. Thus, (benzylcxycarboxyl)-L-valyl-N-[1(S)-[[5-(3-methylbenzyl)-1,3,5-Oxadiazolyl]carboxyl]-2-methylpropyl]-1-prolinamide was prepared and showed Xi = 0.025 mH for inhibition of human neutrophil elastase.

was prepared and showed Ki = 0.025 nM for inhibition of numan neutrophil elastase.

208045-59-4P, CE 2118

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of prolinyl peptide analogs as serine protease inhibitors)
208245-59-4 CAPLUS
214-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[[5-[(3-methyl-henyl]methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/802,765

Page 5

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PI	US 5891				_			0406			199						9961	
	US 5618	792			A		1997										9941	
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	CA 2205	198			C		2002					٠.				•	,,,,,	•••
	CN 1170				Ā		1998			CN	199	5-1	969	52		1	9951	117
	ES 2145				A AA T T A B A1 A AA A2		2000			RS	199	5-6	400	31 31		i	9951 9951 9951 9951	117
	PT 7936				Ť		2000			PT	199	5-6	400	31		î	9951	117
	ZA 9509				Ā		1996			71	199	5-6	919	J.		i	9951	120
	TW 4749				B		2002									•	0051	120
	IL 1160				Ãl		1000			11.	199	5_1	160	79		î	9951 9951	121
	US 5874	585			A		1999	0223		US	199	6-6	985	75		î	9960	915
	US 6015	791			A		1999 2000 1998 1998	0118		US						1	9971	204
	CA 2272	548			AA		1998	0611		CA	199	7-2	272	548 636		î	9971	205
	WO 9824	906			A2		1998	0611		WO	199	7-1	1521	636		î	9971	205
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		DK.	EE.	ES.	FI.	GB.	GE,	GH.	HII.	11	n. T	t.	15	JP.	KK.	YG,	YP.	KD,
		KZ.	LC.	LK.	LR.	LS.	LT,	LU.	I.V.	MI). M	ē.	MK,	MN.	MU,	MY.	NO.	N7
		PL.	PT.	RO.	RU.	SD.	SE,	SG.	SI.	53	τ. 5	ī	TJ.	TM.	TR.	TT.	IIA.	IIG.
		UZ.	VN.	YU.	ZW.	AM.	AZ,	BY.	KG.	KZ	Z. M	D.	RU.	TJ.	TM	•••	,	٠٠,
	RW:	GH.	KE.	LS.	MW.	SD.	52,	UG.	ZW.	AT	r. B	R.	CH.	DE.	nĸ.	FS	PT.	FR.
		GB.	GR.	IE.	IT.	LU.	MC,	NL.	PT.	SI	t. B	F.	BJ.	CF.	CG	CI,	œ,	GA
		GN.	ML.	MR.	NE.	SN.	TD.	TG	,	-	-, -	-,	~,	٠.,	٠٠,	٠.,	٠.,	,
	AU 98558				A1		1998			ΑU	199	8-5	589	4		1	9971	205
	AU 7346	15			B2		2001					•		•		•	/-	
	EP 95452				A2		1999			EP	199	7-9	522	32		1	9971	205
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		IE,	si.	LT.	LV,	FI	RO		,		. •	•		,	,	,	,	,
	CN 12475	542 [°]			A		2000	0315		CN	199	7-1	803	92		11	9971	205
	TR 99016	581			T2		2000	0321						681			9971	
	CN 12475 TR 99016 BR 97134 JP 20015 JP 32200 JP 20017 TR 20016 RU 22177 TW 59334 US 60377 NO 99027 MX 99052 US 1996- US 1996-	584			À		2000	0328		BR	199	7-1	368	4			9971	
	JP 20015	076	79		T2		2001	0612		JP	199	8-5	256	56			9971	
	JP 3220	169			B2		2001	1022						-		•		
	JP 20011	9239	98		A2		2001	0717		JР	200	0-1	974	32		11	9971	205
	TR 20010	3270)		T2		2003	0321		TR	200	1-2	001	32 0327(0		9971	
	RU 22174	136			C2		2003	1127		RU	199	9-1	146	06		1.	9971	205
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	NO 99027	734			A		1999	0802		NO	199	9-2	734	•		1	9990	604
	MX 99052	240			A		2000	0531		MX	199	9-5	240			1	9990	604
PRAI	US 1994-	3458	320		A2		1994	1121								-		
	US 1996-	6985	575		A1		1996	0815										
	US 1996-	7609	916		A		1996	1206										

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse): BSU (Biological
study, unclassified): SFN (Synthetic preparation): THU (Therapeutic use):
BIOL (Biological study): PREP (Preparation): USES (Uses)
(prepn. of fused cycloheptane azole heterocyclic peptoids as serine
protease inhibitors)
20845-59-4 CAPLUS
ZH-1,3-Thiazine-3(4H)-acetamide, dihydro-N-{(1S)-2-methyl-1-{(5-{(3-methyl-phenyl) methyl) n-1,3,4-oxadiazol-2-yl}carbonyl]propyl}-4-oxo-2-phenyl(SCI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 15	CAPLUS	COPYRIGHT	2005	ACS	on ST	N (Continued)
US 1996-761190	λ	1996120	6			,
US 1996-761313	λ	1996120	6			
US 1996-762381	A2	1996120	6			
US 1996-771317	A	1996120	6			
US 1997-984881	Ä	1997120	4			
US 1997-984884	Ä	1997120	i			
US 1997-985056	A	1997120	4			
US 1997-985201	Ä	1997120	4			
US 1997-985298	A	1997120	4			
JP 1998-525656	A3					
WO 1997-US21636	V					
	_		•			
	US 1996-761190 US 1996-761313 US 1996-762381 US 1996-771317 US 1997-984881 US 1997-984884 US 1997-985056 US 1997-985201 US 1997-985298 UJ 1998-525656	US 1996-761190 A US 1996-761313 A US 1996-762381 A2 US 1996-771317 A US 1997-984881 A US 1997-984884 A US 1997-985056 A US 1997-985056 A US 1997-985298 A US 1997-985298 A UF 1997-985286 A3	US 1996-761190 A 1996120 US 1996-761313 A 1996120 US 1996-762381 A2 1996120 US 1996-771317 A 1996120 US 1997-984881 A 1997120 US 1997-984884 A 1997120 US 1997-985056 A 1997120 US 1997-985201 A 1997120 US 1997-985298 A 1997120 US 1997-985298 A 1997120	US 1996-761190 A 19961206 US 1996-761313 A 19961206 US 1996-771317 A 19961206 US 1997-984881 A 19971204 US 1997-984884 A 19971204 US 1997-985056 A 19971204 US 1997-985201 A 19971204 US 1997-985201 A 19971204 US 1997-985208 A 19971204 US 1997-985208 A 19971204	US 1996-761190 A 19961206 US 1996-761313 A 19961206 US 1996-762381 A2 19961206 US 1996-771317 A 19961206 US 1997-984881 A 19971204 US 1997-984894 A 19971204 US 1997-985056 A 19971204 US 1997-985201 A 19971204 US 1997-985228 A 19971204 US 1997-985228 A 19971204 US 1997-985258 A 19971205	US 1996-761190 A 19961206 US 1996-761313 A 19961206 US 1996-762381 A2 19961206 US 1996-771317 A 19961206 US 1997-984881 A 19971204 US 1997-984884 A 19971204 US 1997-985056 A 19971204 US 1997-985208 A 19971204 US 1997-985208 A 19971204 US 1997-985208 A 19971204 US 1997-985208 A 19971204

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

TRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = 0, N, S; at least one of X or Y = N; R1 = alkyl, alkenyl (un) substituted with halo or GH; alkynyl, alkyl-Co2Me, dialkylamino, alkyldialeylamino; cycloalkyl, alkylcycloalkyl, alkyloycloalkyl, C5-12 arylalkyl, cycloalkyl, alkylcycloalkyl, B, alkyl, Alkylhio, alkylthonally, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guandine, carboalkowy, CH, holoalkyl, alkylthio, alkylguandine, dialkylguandine, amidine; B = 502, CO; N6 = fused cycloaptene ring system (0-23) R13, R15 = independently H, alkyl, halo, alkoxy, carboalkowy, cycloalkowy, carboayl, alkylthio, amino, alkylamino or dialkylamino; aryl, fused aryl, cycloalkyl potionally containing 21 O, N, S atcms, and optionally substituted with halo or alkyl; R1 = H, aminoalkyl, alkenyl; (un) substituted cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing 21 N, O, S atcms) and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (RNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysems. R14 = H, aminoalkyl, alkenyl; cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing 21 N, O, S atcms, and optionally substituted with alkyl, halo, alkoyy, oranion, alkylamino, dialkylamino, carboxy, alkylari

Swern oxidation and deprotection gave desired title compound IV. IV inhibited

human neutrophil elastase with Ki = 10.0 nM.
IT 208845-59-4P

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
1999:104503 CAPLUS
130:125411
Preparation of N-substituted derivatives of azole heterocyclic peptoids as serine protease inhibitors
Gyorkos, Alberti Spruce, Lyle W.
Cortech, Inc., USA
U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 345,820.
CODEN: USXXXM
Patent

Patent

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	PA	9115n 18 TENT 	NO.			KIN	D	DATE	:		AP:	PL	I CAT	ION	NO.		D	ATE	
PI	US	5869	455			A	- .	1999	0209		US	1	996-	7613	13		1	 9961	206
	US	5618	792			Α		1997	0408		US	1	994-	3458	20		ī	9941	121
	CA	2205	198			λA		1996	0530		CA	1	995-	2205	198		1	9951	117
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	CN	1170	414			A		1998	0114		CN	1:	995-	1969	52		1	9951	117
	ES	2145	936			Т3		2000	0716		ES	1	995-	9400	31		1	9951	117
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	ZA	9509	819			A		1996	0530		ZA	1	995-	9819			1	9951	120
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	05	28/4	585			•		1999	0223		US	1:	996-	6985	75		11	9960	815
	05	2272	811			Α.		1999	1214		US	1:	997-	9848	84		1	9971	204
	UA.	0024	050 006			12		1998	0611		CA	1:	991-	2212	548		1	9971	205
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			UZ.	VN.	YU.	ZW.	AM.	12.	BY.	KG.	K	7.	MD.	BII	T.I	TM,	11,	UA,	00,
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	AU	9855	894			A1			0629		ΑU	19	-899	5589	4		19	9971	205
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	EP	7346 9545	26			A2		1999	1110		ΕP	19	997-	9522	32		19	9971	205
		R:	λT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GI	λ,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
				SI,	LT,	LV,	FI,	RO											
		1247				A T2			0315		CN	19	97-	1803	92		15	9971	205
	TR	9901	681			T2		2000	0321		TR	19	99-	9901	681		15	971	205
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	JP	3220	169			BZ			1022					. .					
	32	2001	1943	98		A2			0717		JP	Z	100-	1974	32		19 19 19	971	205
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	TU	5022	130			CZ			1127		RU	15	999-	1146	06		15	971	205
	116	6037	225			ь.			0621		110	13	19/-	9011	340		15	19/1	205
	NO.	0037	734			•			0314 0802		US	15	128-	598Z.	,		15	1980	130
	MY	9905	240			^			0531		NU	15	199-	6734			19 19 19	19901	004
PRAT	US	9901: 9713: 2001: 3220: 2001: 2001: 2217: 5933: 6037: 9902: 9905: 1994: 1996:	345	920		12		1994			rın.	13	, , , , - ;	3290			15	,3301	JU4
	US	1996	698	575		A1		1996											
	US	1996	760	916		Ä		1996											
		1996				Ä		1996											
		1996-				ÄZ		1996											
		1996.						1006											

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ANSVER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS On STN US 1997-984881 A 19971204 US 1997-984884 A 19971204 US 1997-985056 A 19971204 US 1997-985201 A 19971204 US 1997-985298 A 19971204 US 1997-985298 A 19971205 US 1997-9821636 B 19971205 US 1997-1205 US 1997-
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The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = 0, N, S; at least one of X or Y = N; Ri = alkyl or alkenyl optionally substituted with halo or hydroxy, alkynyl, alkyl-Co2Me, dialkylamino, alkyldialkylamino; or cycloalkyl, alkylycloalkyl, sikenyleycloalkyl, C5-12 aryl, C5-12 arylakyl, O5-12 arylakenyl optionally containing 1 or more heteroatoms N, S, 0, and optionally substituted; R2, R3 = independently H, alkyl, alkylthio, alkylth

arylalkyl, C5-6 arylalkenyl, cycloslkyl, arylcycloslkyl optionally containing

l or more heteroatoms N, S, O, and optionally substituted; D = bond, CO, amino acid residue; A = bond, CO, NHCO, SO2, O2C, CH2; R14 = H, alkyl, alkenyl, cycloslkyl, aryl, arylalkyl, fused aryl-cycloslkyl optionally containing l or more heteroatoms N, O, S, and optionally substituted, and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, septic shock and multiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysema. HNE-mediated processes are implicated in other conditions such as arthritis, periodotal disease, glomerulonephritis, dermatitis, psoriamis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) ulcers, and invasion behavior of malignant tumors. Thus, oxadiszolyl tripsptoid II (RI - CHZCGHCF3-3), Cbz - PhCH202C) inhibited human neutrophil elastase with Ki = 0.98 nM.

IT 20845-59-49
RI: BAC (Biological activity or effector, except adverse); BSU (Biological scudy, unclassified); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological actudy); PREF (Preparation); USES (Uses) (Dreparation of azole heterocyclic peptoids as serine protease inhibitors)
RN 20845-59-4 CAPLUS
CN 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[(5-[(3-methyl)phenyl)]nethyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(9CI) (CA INDEX NAME)

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 1999:56366 CAPLUS 130:125406
 DN
TI
         130:125406
Preparation of azole heterocyclic peptoids containing keto or diketo ring systems as serime protease inhibitors
Gyorkos, Albert; Spruce, Lyle W.
Cortech, Inc., USA
U.S., 67 pp., Cont.-in-part of U.S. 5,618,792.
CODEN: USXXXM
 DT Patent
LA English
FAN.CNT 18
       US 6656911
PRAI US 1994-345820
US 1996-698575
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ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
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ANSWER 9 OF 15
US 1996-760916
US 1996-761190
US 1996-761313
US 1996-771311
US 1997-984881
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UP 1998-525656
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WO MARPAT 130:12544
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                                                                19961206
                                                                19971204
                                                                19971204
                                                                19971204
19971204
19971204
                                                                19971205
 MARPAT 130:125406
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

TRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE FRINT *

The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptoids I [X, Y = 0, N, S; at least one of X or Y = N, R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-Co2Me, dialkylamino, alkyldialkylamino; or cycloalkyl, salkylcycloalkyl, alkyl-Co2Me, dialkylamino, alkyldialkylamino; or cycloalkyl, c3-12 arylalkenyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted R2, R3 = R*2, R*3 = independently H, alkyl, C5-12 arylalkyl substituted x12, R3 = R*2, R*3 = independently H, alkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with guantidine, carboalkowy, OK, haloalkyl, alkylthio, alkylquanidine, dialkylquanidine or amidine, R11, R12 and K together form a monocyclic or bicyclic ring comprising 5-10 atoms selected from C, N, S, and O; said ring containing 1 or more keto groups; and optionally substituted with halo, cyano, nitro, haloalkyl, amino, aminoalkyl, dialkylquelalkyl, alkenylcylcalkyl, 5-12 arylalkyl, (5-12 arylalkyl, k10; cycloalkyl, alkenylcylcalkyl, c5-12 arylalkyl, c5-12 arylalkyl, (5-12 arylalkyl) comprised the said of human neutrophil elastase (RNE) for the treatment of HNE-mediated processes implicated in conditions such as adult respiratory distress syndrome, spatic shock and miltiple organ failure. A series of studies processes implicated the involvement HNE in myocardial isochemic-reperfusion injury, emphysena. KNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, open transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of walne-derived oxadiazole 11 (R1 = CHICCHHMe-3) (preparation given) with III (Cbr = PhcH2O2C), followed by oxidation of the secondary ale. to the corresponding ketone gave oxadiazole properation; HNE (Ferspeutic use);

208885-59-4P
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SFN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of azole heterocyclic peptoids as serine protease

(Preparation - inhibitors)

RN 208845-59-4 CAPLUS

CN ZH-1,3-Thiazine-3(4H)-acetamide, dihydro-N-((1S)-2-methyl-1-[[5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2005 ACS OD STN (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4	ANSWER 10 OF 15	CAPLUS	COPYRIGHT 2005 ACS on STN	(Continued)
	US 1996-760916	Α	19961206	(**************************************
	US 1996-761190	A2	19961206	
	US 1996-761313	A	19961206	
	US 1996-762381	Ä	19961206	
	US 1996-771317	Ä	19961206	
	US 1997-984881	Ä	19971204	
	US 1997-984884	Ä	19971204	
	US 1997-985056	Ä	19971204	
	US 1997-985201	Ä	19971204	
	US 1997-985298	A	19971204	
	JP 1998-525656	A3	19971205	
	WO 1997-US21636	w	19971205	
os	MARPAT 129:23101	7	155.1200	
GI	123123101	•		

$${}_{R^4-A-Val\text{-Pro-NH}} \underbrace{ \begin{array}{c} {}_{R^2} {}_{R^3} \\ {}_{Y} \end{array} }^{N=X} {}_{R^1}$$

AB The present invention relates to certain substituted oxadiazole, thisdiazole and triazole peptoids I (X, Y = O, N, S) at least one of X or Y = N, R1 = alkyl or alkenyl optionally substituted with halo or hydroxy; alkynyl, alkyl-Co2Re, dialkylamino, alkyldialkylamino; or cycloalkyl, alkyl-Cycloalkyl, alkyl-Cycloalkyl, alkyl-Cycloalkyl, C5-12 arylalkonyl optionally containing 1 or more heteroatoms N, S, O, and optionally substituted, R2, R3 = independently H, alkyl, alkylthio, alkylthio, alkylthio, alkylthio, alkylthio, alkylthio, alkylthio, alkylthio, alkylthio, cycloalkyl, alkylcycloalkyl, Ph, phenylalkyl optionally substituted with quanidine, carboalkowy, OH, halcalkyl, alkylthio, alkylthioalkyl, cycloalkyl, alkylcycloalkyl, cycloalkyl, aryl, arylalkyl, fused aryl-cycloalkyl optionally containing 1 or more heteroatoms N, O, S, and optionally substitutedly, and pharmaceutically acceptable salts thereof, which are useful as inhibitors of human neutrophil elastase (HME) for the treatment of HME-mediated processes implicated in conditions such as adult respiratory distress syndroms, septic shock and miltiple organ failure. A series of studies also have indicated the involvement HNE in myocardial ischemia-reperfusion injury, emphysems. RNE-mediated processes are implicated in other conditions such as arthritis, periodontal disease, glomerulomephritis, dermatitis, portiasis, cystic fibrosis, chronic bronchitis, atherosclerosis, Alzheimer's disease, organ transplantation, corneal ulcers, and invasion behavior of malignant tumors. Thus, coupling of valine-derived oxadiazole II (R1 = CHZCGHMe-3) (preparation given) with Chz-Val-Pro-OH (Chz = PhGHZOCZ), followed by oxidation of the secondary alc. to the corresponding ketone gave oxadiazole peptide derivative III. III inhibited human neutrophil elastase with Ki = 0.025 nM.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

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		7936				Ť			1130					9400				9951	
		9509				Ä			0530					9819			1	9951	12
		4749				В			0201						2388		i	9951	12
	IL	1160	78			A1									78		ī	9951	12
	US	5874	585			T3 A B A1 A		1999	1231 0223					6985			i	9960	81
	US	6159	938			Α			1212					8592			ī	9970	52
		6150				λ		2000	1121					9852			ī	9951 9951 9960 9970 9971	20
	CA	2272	548			λA			0611		CA	19	97-	2272	548		1	9971	20
	¥O	9824	806			A2		1998	0611						636		ī	9971	20
	WO	9824	806			A3		1998	1015		-						•		
		V:	AL,	AM,	AT,		λZ.	BA.	BB,	BG.	BP	١.	BY.	CA.	CH.	CN.	CU.	CZ.	r
			DK.	EE,	ES.	FI.	GB.	GE.	GH,	HU.	ID	Š	IL.	IS.	JP.	KR.	KG.	KP.	ĸ
			KZ.	LC.	LK.	LR.	LS.	LT.	LU.	LV.	MD). I	MG.	MX.	MN.	MV.	MX.	NO.	N
			PL,	PT.	RO,	RU.	SD.	SE.	SG, BY,	SI.	SK	ċ.	SL.	TJ.	TM.	TR.	TT.	UA.	u
			UZ,	VN,	YU,	ZW,	AM,	AZ,	BY,	KG.	KZ	. ,	MD.	RU.	TJ.	TM	,	,	_
		RV:	GH,	KE,	LS,	MW,	SD,	SZ.	UG,	ZW.	AT		BE.	CH.	DE.	DX.	ES.	FI.	F
			GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT.	SE	. :	BF.	BJ.	CF.	CG.	CI.	CM.	Ğ
			GN,	ML,	MR,	NE,	SN,	TD,	TG									,	
	ΑU	9855	894			λ1		1998	0629		ΑU	19	98-	5589	4		1	9971	20
	ΑU	7346	15			B2		2001	0621										
	EP	9545				A2		1999	1110		EP	19	97-	9522	32		1	9971	20
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	١.	IT.	LI.	LU.	NL.	SE.	MC.	P
			IE,	SI,	LT,	LV,	FI,	RO									-		
		1247				Α		2000	0315		CN	19	97-	1803	92		1	9971	20
		9901				T2		2000	0321		TR	19	99-9	9901	681			9971	
		9713				A		2000	0328		BR	19	97-:	1368	4		1	9971	20
	JР	2001	5076	79		T2 B2		2001	0612		JΡ	19	98-!	5256	56		1	9971	20
		3220				B2		2001	1022										
		2001				A2			0717		JΡ	20	00-1	1974	32		1	9971	
		2001		0		T2			0321		TR	20	01-2	2001	32 0327: 06	0	1	9971	20
		2217				C2			1127		***		,,-		•		1	9971	20
		5933				A2 T2 C2 B			0621						8340		1	9971 9971 9971	20
		6037				A			0314		US	19	98-6	5982	3		1	9980	43
		6001				A			1214	1	US	19	98-9	9004	5		1	9980	60
		9902				Α			0802	1	NO	19	99-2	2734			11	9990	60
		9905				A			0531	1	МX	19	99-!	5240			1:	9990	60
PRAI		1994		820		A2 A1		1994											
	US	1996	-698	575		A1		1996	0815										

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 1998:604649 CAPLUS 129:231017

ANSWER 10 OF 15 CAPLUS COFYRIGHT 2005 ACS on STN (Continued) study, unclassified), SFN (Synthetic preparation), THU (Therapeutic use), BIOL (Biological study), PREP (Preparation), USES (Uses) (prepn. of azole heterocyclic peptoids as serine protease inhibitors) 20845-59-4 CAPLUS 20845-59-4 CAPLUS 20847-39-10, APLIANT CONTINUED AND ASSETT OF A CAPLUS CAPLUS AND ASSETT OF A CAPLUS (APLIANT CAPLUS AND ASSETT OF A CAPLUS AND ASSETT OF A CAPLUS CAPLUS AND ASSETT OF A CAPLUS CAPLUS AND ASSETT OF A CAPLUS CA

Absolute stereochemistry.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4	ANSWER 11 OF 15 CA	PLUS COPYRIGHT 200	05 ACS on STN	
AN	1998:585365 CAPLUS			
DN	129:216917			
TI IN	preparation of prol	ine analog peptides	s as serine protease i	nhibitors
PA	Gyorkos, Albert; Sp Cortech, Inc., USA	ruce, Lyle w.		
so	U.S., 62 pp., Cont.	-in-nast of 11 6 1	610 707	
•	CODEN: USXXAM	-In-part of o. s. :	, 618, 792.	
DT	Patent			
LA	English			
FAN.	CNT 18			
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	US 5801148 US 5618792 CA 2205198 CA 1706174 CA 2205198 CN 1170414 ES 2145936 PT 793674 ZA 9509819 TV 474924 IL 116078 US 5598379 CA 2272548 WO 9824806 WO 9824806 WO 9824806 WI AL, AM, AT, DK, EE, ES, XZ, LC, LK, PL, PT, RO, UZ, VN, YU, PT, RO, UZ, VN, YU, CY, VN, YU, CY, VN, YU, CY, VN, YU, YN, YU, YN			
F1	US 5619702	A 19980901 A 19970408	US 1996-771317	19961206
	CA 2205198	AA 19960530	US 1994-345820 CA 1995-2205198	19941121
	CA 2205198	C 20020604	CA 1995-2205198	19951117
	CN 1170414	A 19980114	CN 1995-196952	10051117
	ES 2145936	T3 20000716		19951117 19951117 19951117 19951120 19951120 19951121
	PT 793674	T 20001130	PT 1995-940031	19951117
	ZA 9509819	A 19960530	78 1005-0010	19951120
	TW 474924	B 20020201	TW 1995-84112388	19951120
	IL 116078	A1 19991231	IL 1995-116078	19951121
	US 5874585	A 19990223	US 1996-698575	19960815 19971204
	US 5998379	A 19991207	US 1997-985056	19971204
	CA 2272548	AA 19980611	CA 1997-2272548	19971205
	WO 9824806	A2 19980611	TW 1995-84112388 IL 1995-116078 US 1996-698575 US 1997-985056 CA 1997-2272548 WO 1997-US21636	19971205
	WO 9824806	A3 19981015		
	W: AL, AM, AI,	AU, AZ, BA, BB, BG	, BR, BY, CA, CH, CN,	CU, CZ, DE,
	VA, EE, ES,	ID IC IT IN IN	J, ID, IL, IS, JP, KE, J, MD, MG, MK, MN, MW,	KG, KP, KR,
	PL. PT. RO.	RIT. SD. SE. SG ST	, SK, SL, TJ, TM, TR,	MX, NO, NZ,
	UZ. VN. YU.	ZW. AM. AZ. BY. KG	KZ, MD, RU, TJ, TM	11, UA, UG,
	RW: GH, KE, LS.	MW. SD. SZ. UG. ZW	, AT, BE, CH, DE, DK,	ES FI FR
	GB, GR, IE,	IT, LU, MC, NL. PT	, SE, BF, BJ, CF, CG,	CI. CM. GA.
	GN, ML, MR,	NE, SN, TD, TG		,,,
	AU 9855894	A1 19980629	AU 1998-55894	19971205
	AU 734615	B2 20010621		
	FL 324270		EP 1997-952232	19971205
	R: AT, BE, CH,	DE, DK, ES, FR, GB	GR, IT, LI, LU, NL,	SE, MC, PT,
	IE, SI, LT, CN 1247542		ent 1000 100000	
	TR 9901681	A 20000315 T2 20000321	CN 1997-180392	19971205
			TR 1999-9901681 JP 1998-525656	19971205 19971205
	JP 3220169	B2 20011022	01 1330-323036	133/1203
	JP 2001192398	A2 20010717	JP 2000-197432	19971205
•	TR 200103270	T2 20030321	JP 2000-197432 TR 2001-200103270 RU 1999-114606	19971205
	RU 2217436	C2 20031127	RU 1999-114606	19971205
	JP 2001507679 JP 3220169 JP 2001192398 TR 200103270 RU 2217436 TV 593340 US 6037325 US 6100238 NO 9902734 MX 9905240 US 1994-345820 US 1996-698575 US 1996-69166	B 20040621	TW 1997-86118340 US 1998-69823 US 1998-89587 NO 1999-2734 MX 1999-5240	19971205
	US 6037325	A 20000314	US 1998-69823	19980430
	US 6100238	A 20000808	US 1998-89587	19980603
	NO 9902734	A 19990802	NO 1999-2734	19990604
222	MX 9905240	A 20000531	MX 1999-5240	19990604
PRAI	US 1994-34582U	A2 19941121		
	US 1996-760916	A1 19960815 A 19961206		
	US 1996-761190	A 19961206 A 19961206		
		13301600		

ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) 2H-1,3-Thiazine-3(4H)-acetamide, dihydro-N-[(15)-2-methyl-1-[[5-{(3-methyl-1-n-1),act-yl-1-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-(SCI) (CA INDEX NAME)

THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT RE.CNT 32

L4	ANSWER 11 OF 15	CAPLUS	COPYRIGHT 2005	ACS on STN	(Continued)
	US 1996-761313	A	19961206		,
	US 1996-762381	A	19961206		
	US 1996-771317	A2	19961206		
	US 1997-984881	A	19971204		
	US 1997-984884	λ	19971204		
	US 1997-985056	λ	19971204		
	US 1997-985201	Ä	19971204		
	US 1997-985298	Ä	19971204		
	JP 1998-525656	A3	19971205		
	WO 1997-US21636	¥	19971205		
GI					

Proline analog peptides I and II [X, Y = 0, N, S; Rl = alkyl, alkenyl, alkynyl, dialkylamino, etc.; R2, R3 = H, alkyl, alkylthio, alkylthioalkyl, etc.; B = SO2, CO; 21, 22 = direct bond or CH2; D = direct bond or certain amino acid residues; A = CO, NHCO, SO2, COC, O2CNH, CH2; R14 = H, alkyl, alkenyl, cycloalkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, alkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, alkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, alkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, alkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, dialkylamino, alkyl, aryl, arylalkyl, etc.; W = S, O; R8 = alkylamino, etc. Thus, (benzyloxycarbonyl)-1-L-yalyl-N-[1-1(-2[-5]-G)-methylhenyl]-1-T, arylaryl)-1-T, arylaryl-1-C-prolinamide, prepared from 3-(S)-([benzyloxycarbonyl) amio-2-acetoxy-4-methylpentamenitrile, 3-methylphenylacetic hydrazide, and Cbz-Val-Pro-OH, showed inhibition activity Ki = 0.025 nM.
208845-59-4P
KL: BAC (Biological activity or effector, except adverse): BSU (Biological study, unclassified): SPN (Synthetic preparation): THU (Therapeutic use): BIOL (Biological study): PREP (Preparation): USES (Uses) (preparation of proline analog peptides as serine protease inhibitors) 208845-59-4 CAPLUS

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN 1998:394350 CAPLUS 129:68032 Preparation of oxadiazole peptide analogs as serine protease inhibitors Gyorkos, Albert; Spruce, Lyle W. Cortech, Inc., USA; Gyorkos, Albert; Spruce, Lyle W. PIXXD2 Preparation 187 pp. CODEN: PIXXD2 CODEN: P DT Patent LA English FAN.CNT 18 PATENT NO. KIND A2 A3 DATE 19980611 19981015 APPLICATION NO. DATE WO 9824806 WO 9824806 WO 1997-US21636 19971205 A1 1980629 A1 1997-22.734 19971205
B2 20010621
A2 19991110 EP 1997-952232 19971205
DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, HC, PT,
LV, FI, RO
A 20000328 BR 1997-13684 19971205
B2 20010612 JP 1998-52565 19971205
B2 20011022 JP 1998-525656 19971205
B2 20011022 JP 1998-525656 19971205
B2 20031207 RU 1999-114606 19971205
A 19990802 NO 1999-2734 19990604
A 20000331 HX 1999-5240 199910604
A1 20030327 US 2001-928117 20010810
B2 20031202 A 19961206
A 19961206
A 19961206
A 19961206
A 19961206
A 19961206
A 19971204
A 19971205

MARPAT 129:68032

The present invention relates to certain substituted oxadiazole, thiadiazole and triazole peptide analogs I [X, Y = independently O, S, (un) substituted N; Z = serine protease binding moiety, Preferably a human neutrophil elastase binding moiety, Rl = (un) substituted alkyl, alkenyl, alkynyl; OH, amino, alkylamino, dialkylamino, cycloalkyl, alkylcycloalkyl, alkylcycloalkyl, alkylcycloalkyl, alkynylcycloalkyl, alkynylcycloalkynyl, C5-12 arylalkyl, C5-12 arylalkenyl, fused C5-12 arylcycloalkyl, alkynylcycloalkynyl, shif nare useful as inhibitors of serine proteases. Thus, Swern oxidation of reduced pseudopeptide II (2 = PhcH2O2C), prepared in 8 steps from 35-(benzyloxycarbonylamino)-2-acetoxy-4-methylpentanenitrile, 3-methylphenylacytic bydrazide, and Z-Val-Pro-OH, gave 74% desired oxadiazole III. III inhibited human neutrophil elastase with IC50 = 0.025 nM in an in vitro assay.

208845-55-49

RL: BAC (Biological activity or effector, except adverse): BSU (Biological study, unclassified): SPN (Synthetic preparation): TRU (Therapeutic use): [BIO. (Biological activity): PREP (Preparation): USES (Uses) (preparation of oxadiazole peptide analogs as serine protease and human neutrophil elastase inhibitors)

208845-59-4 (CAPLUS 2H-1,3-7hiazine-3(4H)-acetamide, dihydro-N-[(1S)-2-methyl-1-[(5-[(3-methylphenyl)methyl]-1,3,4-oxadiazol-2-yl]carbonyl]propyl]-4-oxo-2-phenyl-lytte stereochemistry.

Absolute stereochemistry.

71:9716 CAPLUS
71:971

DT LA AB Italian
The antioxidant effect of title compds. toward vitamin C, at 60°,
was in the following decreasing order: 2-phenyl-3-(R-substituted)-5-(Rlsubstituted) thiazolidin-4-one (1) (R = piperidin-3-yl, Rl = H), I (R = 2-methylpiperidin-6-yl, Rl = H), I (R = 3-methylpiperidin-6-yl, Rl = H), I (R = 3-methylpiperidin-6-yl, Rl = H), 2-phenyl-3-(R-substituted) tetrahydro-1, Rl = H), 2-phenyl-3-(R-substituted) tetrahydro-1, 3-thiazin-4-one (II) (R = piperidin-3-yl, Rl = H), I (R = piperidin-2-yl, Rl = H), I (R = piperidin-6-yl, Rl = H), II (R = NHOCOSHM, Rl = H), II (R = NHOCOS

10165-03-4

RL: BIOL (Biological study)
(antioxidant activity of)
10165-03-4 CAPUS
4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA
INDEX NAME)

ΙT

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN AN 1966:423765 CAPLUS DN 65:23765 CREF 65:4439h, 4440a-b
TI Relation of chemical structure. AU Fenech, Giovanne SO Atti dell'

Relation of Chemical structure to activity of heterocyclic sulfates Fenech, Glovania and Atti della Societa Peloritana di Scienze Fisiche, Hatematiche e Naturali (1965), 11(1-2), 117-29 (CODEN: ASPSAJ) 158N 0037-8860

Journal

CODEN: ASPAJ; ISSN: 0037-8860
Journal
Journal
Lalian
The antibacterial and pharmacol. effects of a series of thiazolidinones and metathiazanones were studied. Twenty-six compds. with and without ortho, meta, and para substitution of Cl or NO2 on the phenyl ring and a 2-, 3- or 4-pyridyl ring or an isonicotinoylamino moiety on the N of the thiazole and metathiazanone rings were tested. Oral doses of 25-300 mg./kg. of various compds. were given rats kept under observation for characteristic central nervous system (CMS) effects. Antibacterial effects were followed by the agar diffusion technique using 6.3-mm. filter paper disks saturated with suspensions containing 20 y/al of the compds. studied. Of the metathiazanones, 2-phenyl-3-(3-pyridyl)-1,3-thiazan-4-one and 2-phenyl- and 2-(2-chlorophenyl)-3-(4-pyridyl)-1,3-thiazanione had stimulating effects on the CNS at doses >50 mg./kg., characterized by tremors and tonic convulsions. A depressing action was noted at lower dose lavels. Of the thiazolidinones studied 2-(3-nitrophenyl)-3-(3-pyridyl)-4-thiazolidinone had a weak CNS stimulating effect and 2-(2-chlorophenyl)-and 2-(3-nitrophenyl)-3-(1-pyridyl)-1,3-thiazan-4-one had a weak inhibiting effect and thiazolidinone had CNS depressing effects. Only 2-(2-nitrophenyl)-3-(2-pyridyl)-1,3-thiazan-4-one had a weak inhibiting effect on Staphylococcus aureus and Trichophython mentagrophytes. The 6-membered Sheterocyclic ring, the unsubstituted phenyl ring, and the 4-pyridyl radical produced the greatest CNS effect.

10165-03-4, 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (pharmacology of)

(pharmacology of)

10165-03-4 CAPLUS

4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI)

(CA INDEX NAME)

4H-1,3-Thiszin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)

10165-04-5 CAPLUS
4E-1,3-Thiszin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)

ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

L4 ANSVER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1962:66924 CAPLUS
D1 56:66924
CREF 56:12898-9
I Reactivity of the azomethine group. XI. Synthesis of 2-aryl-3-(3- and 4-pyridyl)-1,3-thiazan-4-ones
AF Penech, Giovanna, Basile, Maria
CS Univ. Messina, Italy
Gazzetta Chinica Italiana (1961), 91, 163-72
CODEN: GCITA9, ISSN: 0016-5603
J Journal
LA Unavailable
AB Reactions of Schiff bases from 3- and 4-aminopyridine with HS(CH2)2CO2H
(I) were described. I and the Schiff base from 3-aminopyridine and B2H
refluxed in dry C6H6 70 hrs., gave 2-phenyl-3-(3-pyridyl)-1,3-thiazan-4one, m. 105-7', together with some S(CH2CHZCOZH)2 and benzaldsbyde
thioactela. The following 1,3-thiazan-4-ones were similarly obtained:
2-(2-chlorophenyl)-3-(3-pyridyl), m. 110-12', 2-(3-nitrophenyl)-3(3-pyridyl), n. 152-4', 2-phenyl-3-(4-pyridyl), m. 190-1',
2-(2-chlorophenyl)-3-(4-pyridyl), m. 201-3' With p-02NCSH4CHO, no
cyclic compound was obtained. With m-02NCSHCHO and I in the presence of
4-aminopyridine a mixture of products was obtained, including a 1:1 compound
of the acid and aldebyde.

IT 10185-03-4 (AFL). 3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4pyridyl) n. 10165-04-6, HR-1,3-Thiazin-4-one, 2-(ochlorophenyl) tetrahydro-3-(4-pyridyl)(preparation of)
RN 10165-03-4 (AFLUS
CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI)
NDEX NAME)

10165-04-5 CAPLUS
4H-1,3-Thiazin-4-one, 2-{o-chlorophenyl}tetrahydro-3-(4-pyridyl)- {7CI, 8CI} (CA INDEX NAME)

L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

10/802,765

Page 11

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FILE 'CAOLD' ENTERED AT 12:09:13 ON 14 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907-1966 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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=> s 13

L5

2 L3

=> d 1-2 all hitstr

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LS ANSWER 1 OF 2 CAOLD COPYRIGHT 2005 ACS on STN

AN CA65:4439h CAOLD

relation of chemical structure to activity of heterocyclic sulfates

AV Fenech, Giovanna

IT 10164-84-8 10164-95-9 10164-86-0 10164-87-1 10164-88-2 10164-99-3

10164-90-6 10164-97-3 10164-93-8 10164-93-9 10164-94-0 10164-95-1

10165-96-2 10164-97-3 10164-93-6 10164-93-9 10165-00-1 10165-01-2

10165-02-3 10165-03-4 10163-04-5 10249-17-9

10249-19-1 10249-19-1 10249-20-4 10249-21-5 10254-52-1

IT 10165-03-4 CAOLD

CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)
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V Ph

RN 10165-04-5 CAOLD
CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)

L5 ANSWER 2 OF 2 CAOLD COPYRIGHT 2005 ACS on STN
AN CAS6:128989 CAOLD
TI SUlfinic acid amidines - (I) preparation of sulfinic acid amidines from anidine
derivs. and their cyclization to 1,2,4,6-thiatriazines
AU Goerdeler, Joachim Wedekind, B.
11 10165-03-4 10165-04-5 53245-14-0 97339-63-4
97379-78-7 97394-35-9 98028-89-8 98780-16-6 98780-17-7 99671-37-1
99801-23-7 99801-23-8 100146-98-3 100149-31-3 100153-92-2 100174-69-4
100260-05-7 100353-02-8 100457-20-3 100457-21-4 102960-78-1 106172-78-5
RN 10165-03-4 CAOLD
CN 4H-1,3-Thiazin-4-one, tetrahydro-2-phenyl-3-(4-pyridyl)- (7CI, 8CI) (CA

RN 10165-04-5 CAOLD
CN 4H-1,3-Thiazin-4-one, 2-(o-chlorophenyl)tetrahydro-3-(4-pyridyl)- (7CI, 8CI) (CA INDEX NAME)

10/802,765 Page 13

=> fil capl
FILE 'CAPLUS' ENTERED AT 12:09:35 ON 14 APR 2005
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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'.FIONA' IS DEFAULT FORMAT FOR 'CAPLUS' FILE

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L4

(FILE 'HOME' ENTERED AT 12:07:18 ON 14 APR 2005)

FILE 'REGISTRY' ENTERED AT 12:07:30 ON 14 APR 2005 L1 STRUCTURE UPLOADED

L2 0 S L1

L3 8 S L1 FULL

FILE 'CAPLUS' ENTERED AT 12:08:11 ON 14 APR 2005 15 S L3

FILE 'CAOLD' ENTERED AT 12:09:13 ON 14 APR 2005 L5 2 S L3

FILE 'CAPLUS' ENTERED AT 12:09:35 ON 14 APR 2005 E SUN OUN/AU

L6 134 S E3

E KYLE DONALD/AU

L7 91 S E6-E7 L8 200 S L6 OR L7

L9 11 S L8 AND THIAZ?

=> d que 19 stat

L6 134 SEA FILE=CAPLUS ABB=ON PLU=ON "SUN QUN"/AU

L7 91 SEA FILE=CAPLUS ABB=ON PLU=ON ("KYLE DONALD J"/AU OR "KYLE

DONALD JAMES"/AU)

L8 200 SEA FILE=CAPLUS ABB=ON PLU=ON L6 OR L7

L9 11 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND THIAZ?

- AN TI AU
- ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN 2006:657939 CAPLUS Quinacolinones and benzothiazinones as novel sodium channel blockers Victory, Sam F.; Sun, Qun; Limberis, Jim; Eyle, Donald
- J. Discovery Research, Purdue Pharma, L.P., Cranbury, NJ, 08512, USA Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-075 Publisher: American Chemical Society, Washington, D. C. CODEN: 69FT28
- Conference: Meeting Abstract
- CODEN: 69FT28
 Conferences Heeting Abstract
 English
 V102262 is a potent state-dependent sodium channel blocker (Xi = 370 nM, rBIIa) that has been shown to be efficacious in the Chung model of neuropathic pain. Toward the discovery of a second-generation compound having an improved pharmaceutical profile, we embarked on a systematic structure-activity investigation simed at replacing the semicarbazone molety of V102862 with various heterocycles as a bioisosteric replacement. Our labs. have reported on several series of high affinity sodium channel blockers as part of this effort, including a series of compds. containing a thiasolidinone ring system as a replacement. Some of the most potent compds. in the thiasolidinone series possessed a hydrophobic aryl ether moiety, similar to V102862, and also a piperidinylethylamine moiety. To further explore the bioisosteric replacement of the semicarbazone moiety of V102862, several addnl. series of compds. were synthesized including those having a quinazolina (3H)-one or a 2,3-dihydro-benzothizin-4-one core ring system. Within each of these new series, the optimized piperidinylethylamine group of the thiasolidinone series was held constant while the hydrophobic aryl ether moiety was varied, generating potent sodium channel blockers in each series. Details of the synthesis and SAR of analogs will be presented.

- ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN 2004:20339 CAPLUS 140:77163 Preparation of thiazolylpiperezines for treating or preventing

- pain Kyle, Donald J.; Sun, Qun
 USA
 U.S. Pat. Appl. Publ., 37 pp., which
 CODEN: USXXXCO
 Patent
 English
 CNT 2

FAN.	CNI Z				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PΙ	US 2004006091	A1	20040108	US 2003-374863	20030227
PRAI	US 2002-360172P	P	20020301		
	US 2002-411084P	P	20020917		

MARPAT 140:77163

The title compds. [I, Rl = Me, halo, R3 = alkyl, alkenyl, alkynyl, etc., R4 = H, R5 = alkyl, cycloalkyl, aryl, etc., n = 0-2; X = 0, S], useful for treating or preventing pain in a patient, were prepared E.g., a multi-step synthesis of three title compds. II [R = 4-tert-butylphenyl, and 4-trifluoromethylphenyl], was given. The compds. I were tested for binding to the human WR1 receptor. Typically, the compds. I have an ICSO of < 25 μ M for inhibition of capsaicin-induced activation. Assays for testing binding of the compds. I to mGluR3 and to mGluR1 are described (no data). Pharmaceutical composition comprising the compound I is claimed.

- ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN 2004:657937 CAPLUS Design and synthesis of novel potent aryl substituted benzimidazoles socium channel blockers thou, Xisocaing, Fun, Qun, Eyle, Donald J., Ilyin, Victor, Limberts, Jim Discovery Research, Purdue Pharma L.P., Crambury, NJ, 08512, USA Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-073 Publisher: American Chemical Society, Washington, D. C. CODEN: 699728
 Conference, Heeting Abstract English
 V102862 is a state-dependent sodium channel blocker that is efficacious in animal models of neuropathic pain. However, an in vivo metabolism study in rats suggested that the semicarbazone moiety of V102862 could account for formation of toxic semicarbazide metabolites. In order to improve potency and pharmaceutical profile, a focused chemical library with various substituted thiaxolidinones was prepared The lead compound I was identified with a Ki of 90 nM for state-dependent inhibition of Nav1.2 (rBIIa Na) channels co-expressed with beta 1 subunit in Xenopus occytes. Further modification of the thiaxolidinone compound 1 led to a series of novel potent aryl substituted benzimidazoles (e.g. 2) as sodium channel blockers.

- ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
 2003:634845 CAPLUS
 Parallel synthesis of a biased library of thiazolidinones as a
 novel sodium channel antagonists
 Tafesse, Laykea; Sun, Qun; Limberts, James T.; Islam, Khondekar;
 Ryle, Donald J.
 Purdue Pharma LP, Cranbury, NJ, 08512, USA
 Abstracts of Papers, 226th ACS National Meeting, New York, NY, United
 States, September 7-11, 2003 (2003), MEDI-237 Publisher: American Chemical
 Society, Washington, D. C.
 CODEN: 69EKY9
 Conference; Meeting Abstract
- CODEN: 69EXY9
 Conference: Meeting Abstract
 English
 A biased chemical library containing 91 differentially substituted
 thiasoldidnones was prepared in an effort to improve the pharmacol.
 and to overcome certain development liabilities of a known anticonvulsant
 agent V102862. The collection was prepared in a single step multi-component
 condensation reaction that produced good yields and very high crude purity
 (751-85%). Seven compds., identified within the library were shown to be
 more potent than V102862, our parent reference compound, in an
- rophysion. assay measuring sodium channel antagonism. The most potent compound, 3-(2-piperidinylethyl)-2-(3-(3-trifluoromethylphenoxy)phenyl) thiazolidinone, has a Ki of 90 mM.

```
ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
2003:625433 CAPLUS
140:93967
Parallel synthesis of a biased library of thiexelidinones as novel sodium channel antagonists
Sun, Qun, Tafesse, Laykear Limberis, James T., Islam, Khondekar, Ryle, Donald J.
Purdue Pharma LP, Cranbury, NJ, 08512, USA
Combinatorial Chemistry and High Throughput Screening (2003), 6(5), 481-488
CODEN: CCMSTU, ISSN: 1386-2073
Bentham Science Publishers Ltd.
Journal
English
    English
CASREACT 140:93967
```

AB A biased chemical library containing 91 differentially substituted thiszolidinones, e.g., I, was prepared in an effort to improve the pharmacol. of a known anticonvulsant agent V102862. The collection was prepared in a single-step multicomponent condensation reaction that produced the thiszolidinones in good yields and very high crude purity. Seven compds., identified within the library, were shown to be more potent than V102862, our parent reference compound, in an electrophysiol. assay measuring sodium channel antagonism. The most potent compound (I) has a Ki of 90 nM.

RE.CNI 25 THERE ARE 25 CITED REFERENCE TO THIS RECORD

. THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) amelioration of both acute and chronic pain, of depression, as local anesthetics, as antiarrhythmics and for the treatment or prevention of diabetic neuropathy. The compds. of the invention are sodium channel blockers. RE.CNT

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI IN PA SO DT LA	Aryl-su Sun, Qu Euro-Ce PCT Int CODEN: Patent English	ltiq . Ap PIXX	yle, ue, pl.,	Don S.A.	ald d , Lu:	J.			a th	erap	encı	c us	e th	ereo	r		
PAN.	CNT 1 PATENT				KIN	D	DATE			APPL	CAT	ION	NO.		D	ATE	
PI	US 2003 EP 1417 R: JP 2004	0083 AE, CO, GM, LS, PL, UA, TJ, GH, CH, NE, 1095 187 AT, IE, 5382	98 AG, CR, HR, LT, UG, TM GM, CY, SE, SN, 21 BE, SI, 85	AL, CU, HU, LU, RO, US, KE, CZ, SK, TD,	AM, C2, ID, LV, RU, UZ, LS, DE, TR, TG A1 A1 DE, LV,	AT, DE, IL, MA, SD, VN, DK, BF,	2003 AU, DK, IN, MD, SE, YU, MZ, EE, BJ, 2003 2004 ES, RO, 2004	AZ, DM, IS, MG, SG, ZA, SD, ES, CF, 0612 0512 FR, MK, 1224	BA, DZ, JP, MK, SI, ZM, SL, FI, CG,	BB, EC, KE, MN, SK, ZW, SZ, FR, CI, US 20 GR,	BG, EE, KG, MW, SL, AM, TZ, GB, CH,	BR, ES, KP, MX, TJ, AZ, GR, GR, GA, 1955 7632 LI, BG,	BY, FI, KR, MZ, TM, BY, ZM, IE, GN, 30 75 LU, CZ,	GB, KZ, NO, TN, KG, ZW, IT, GQ,	CA, GD, LC, NZ, TR, KZ, AT, LU, GW,	GE, LK, OM, TT, MD, BE, MC, ML,	CN, GH, LR, PH, T2, RU, NL, MR, 716 716 PT,
PRAI OS GI	US 2004 US 2001 US 2002 WO 2002 MARPAT	-305 -195 -US2	099P 530 2367		A1 P A3 W		2004 2001 2002 2002	0716 0716		US 2	004-	8027	65		2	0040	318

The invention discloses aryl-substituted thiaxolidinones I [n = 1, 2r Rl = YN(R3)(R4) (Y = alkylene; R3, R4 = H, alkyl, aryl, or R3 and R4 together form alkylene chain having 4-5 C optionally interrupted by N or O), pyridylalkyl, optionally substituted piperidin-4-yl; R2 = optionally substituted phenoxyphenyl, optionally substituted phenylthiophenyl, optionally substituted benzyloxyphenyl, etc.], or a pharmaceutically acceptable salt or solvate thereof. The invention also discloses the use of I for the treatment of neuronal damage following global and focal ischemia, for the treatment or prevention of neurodegenerative conditions, e.g. amyotrophic lateral sclerosis, and for the treatment, prevention or

19 ANSVER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
AB A-B-C-D-E-F-G-H-I-J-C-E (A = H, D- and L- Arg, Gln, Asn, Lys, Sar, N-e-Ac-Lys, NG-p-tosyl-Arg, NG-NO2-Arg, Lys-Lys, Ac-Arg, citrullines B = bond, D- and L- Arg, Gln, Asn, Lys, Sar, Ne-Ac-Lys, NG-p-tosyl-Arg, NG-NO2-Arg, Ac-Arg, citrullines C = bond, Fro, 6Hyp, Olc, dehydroFro, Tic, Aoc, L-azetidine-2-carboxylate, Eac, Gly, Thz, Aib, D = 2-pyrrolidinyl, Fro, 4Hyp, Olc, dehydroFro, Tic, Aoc, L-azetidine-2-carboxylate, Eac, Gly, Thz, Aib, D = X(GU2)azl(GH2)cdHCO) X = bond, NH; 21, 22 = bond, C3-8 carbocycle residue, (cyclic) alkenylenes Y = H, CH2OH, alkyl, PbcH2, thiophenylmethyl, furylnethyls = n, n = 0-12; metho 512; F = bond, aromatic amino acid, G = bond, Sar, Thr, Gly, Val, Ala, Cys, Tyr; H = D-aromatic
anino acid, D-Hype; I = Olc, Aoc, Thz, Tic, L-indoline-2-carboxylic acid, Aib, Leu, Ile, Val, Thi, octahydro-lH-isoindole-1-carboxylate, pipecolinic acid, Fro, 6Hyp, azetidine-2-carboxylate, Phe, homoPbe, Hype; J = Arg, Orn, Asn, Gln, Hys; Hype = Ql; R = (substituted) alkyl, cycloalkyl, aryl, aralkyl, etc.; X = O, S, SO, SO2; Cn = OH, anide, alkoxy, D- or L- amino acid residues Aib = 2-aminoisobutyrate; Aoc = (S, S, S)-2-azabicyclo[3.3.0]octane-3-carboxylate; Eac = -aminocaproate; dehydrofro = 3,4 dehydroproline; 6Hyp = 4-hydroxyproline; Thi = β-2-thienylalanine; Thz = thiaxolidine-4-carboxylate; Tic = tetrahydroisoquioline-3-carboxylate; oic = (2S, 38,7AS)-octahydro-H-indole-2-carboxylate], were prepared Thus, title compound (I) antagonized bradykinin with Ki = 15 μM.

ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) from L- and D-isomers of Arg, Gln, Asn, Lys; C is a C2 to C18 olefinic aminoalkencyl NH(CM2)m21(CM2)m22(CM2)c00 wherein 21 and 22 are independently selected from the group consisting of a bond, C3-8 carbocycle, C2-18 monoelefin or C4-18 polyolefin cont; 1-5 double bonds which may optionally be incorporated into a cyclic system; m, n, and o are independently 0-12; with the proviso that their total does not exceed 16; D is a bond or is selected from Ser, Thr. Gly, Val, Ala, Cys, and Tyr; E is selected from the group consisting of a D-arom, amino acid and a D-Hype (bydrowyproline ether/Chiosther); F is selected from, e.g., Oic, Aoc, Thr. Tic (Oic is (25,3a5,3a5)-octahydro-IH-indole-2-carboxylic acid; Aoc is (5,5,5)-2-azabicyclo[3.3,0) octans-3-carboxylic acid; Thz is carboxylic acid; C3 (25,3a5,3a5)-octahydro-IH-indole-2-carboxylic acid; Aoc is (5,5,5)-2-azabicyclo[3.3,0) octans-3-carboxylic acid; Thz is carboxylic acid; Tic is tetrahydroisoquinoline-3-carboxylic acid; G (3,5a5) carboxylic acid; Tic is tetrahydroisoquinoline-3-carboxylic acid; Tic is tetrahydroisoquinoline-3-carboxylic acid; Tic is carboxylic acid; Tic is a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acids at at positions 2 through 5 are replaced by olefinic aminoalkencyl groups to reduce the peptide nature of the compds. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites. Thus, e.g., pseudopeptide I was prepd. by solid-phase methodol., incorporating aminoalkencyl spacer N-Boc-3-[2-(aninomethyl))phenyl]-2-propencic acid (180 prepd.); I exhibited binding to human bradykinin B2 receptor with K = 27 nM, and bradykinin antagonist activity with pA2 = 120 ± 8.

	MISSER O OF II CAP	103 CO.	rikiuni 2	002 VC2 OU 21H	
AN	1996:494750 CAPLUS				
DN	125:196389				
TI	Bradykinin antagoni	st pseu	dopentide	derivatives of amino	alkenoic acids
IN	Eyle, Donald J.	•			
PA	Scios Nova Inc., US.				
50	U.S., 26 pp., Cont.		17 .	E 444 046	
-	CODEN: USXXXAM	-In-bat	C 01 U.S.	3,444,046.	
-					
DT	Patent				
LA	English				
FAN.	CNT 7				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5541286	A	19960730	US 1994-281907	19940728
	US 5521158	Ä	19960528		19921008
	US 5444048	Ä		US 1993-118981	19930909
	CA 2171446	ÄÄ	19950316		19940909
	CA 2171446	č	20041123		19940909
	WO 9507294				
		A1	19950316	WO 1994-US10128	19940909
	W: CA, JP, US				
	RW: AT, BE, CH,		, ES, FR,	GB, GR, IE, IT, LU,	
	EP 716661	A1	19960619		19940909
	EP 716661	B1	20000405		
	R: AT, BE, CH,	DE, DK,	ES, FR,	GB, GR, IE, IT, LI,	LU, MC, NL, PT, SE
	JP 11500100	TZ	19990106	JP 1994-508795	19940909
	AT 191486	E	20000415	AT 1994-929158	19940909
	ES 2148347	T3	20001016	ES 1994-929158	19940909
	US 5817756		10001006	11C 1005 401505	19950309
	US 5610142	Ä	19970311	US 1995-416524	19950403
PRAT	US 1992-957879				19930403
	US 1993-118981	A2	19930909		
	US 1993-118550	^2	19930909		
	US 1993-118558	À	19930909 19930909		
		A	19930909		
	US 1993-119341	A	19930909 19940728		
	US 1994-281904	λ	19940728		
	US 1994-281906	λ	19940728 19940728		
	US 1994-281907	λ	19940728		
	US 1994-281908	A	19940728		
	US 1994-119341	A	19940909		
	WO 1994-US10128	¥	19940909		
	US 1994-353426	B2	19941209		
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L9 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

Pseudopeptide compds. A-B-C-D-E-F-G-Cn wherein: A is H or is selected from L- and D-isomers of, e.g., Arg, Gln, Asn, Lys; B is a bond or is selected

Ser-D-Tic-Oic-Arg-OH

H-D-Arg-Arg-NH-

H-D-Arg-Arg-Eys-Pro-Gly-Cys-Ser-D-Tic-Oic-Arg-OH I

H-Al-A2-A3-A4-A5-A6-R1 [Al, A2 = D- or L-Arg, -Gla, -Asa, -Lys(Ac), -Lys, Lys-Lys, Sar, etc.; A3 = Ql, Q2; Y, Z = amino acid residues forming covalent bonds through their side chains; D, E = Pro, 4Hyp, Tic, Ala, Gly, Oic, Thz, Alb, dehydroprolyl, etc.; F = Phe, Thi, Trp, Tyr, Leu, Ile, Tic, Oic, hPhe, Nal, Val, phenylglycyl, etc.; G = bond, Ser, Thr, Gly, Val, Ala, Cys, Tyr, A4 = D-Phe, D-Tic, D-Pro, Q3; R = H, (substituted) alkyl, aryl, aralkyl, alkenyl, cycloalkyl, etc.; X = O, S, SO, SO2; A5 = Oic, Aoc, Tic, Pro, Alb, Leu, Ile, Val, Thi; Phe, hPhe, Q3, etc.; A6 = Arg, Orn, Asa, Gln, Lys, R1 = GH, amide, alkoxy, D- or L-amino acid or peptide residue; 4Hyp = 4-hydroxyprolyl; hPhe = homophenylalanyl; Thi = B-2-thienylalanyl; Tic = tetrahydroisogulonin-3-carboxylic acid residue; Oic = (2S, 3a5, 7a5)-octahydro-Hi-indole-2-carboxylic acid residue; Alb = 2-aminoisobutyric acid residue; Alb = 2-aminoisobutyric acid cresidue, were prepared Thus, title compound (I; prepared using FMOC chemical) antagonized bradykinin in guines pig intestinal strips with pA2 = 6.6.

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ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
1995:339374 CAPLUS
123:9926
Preparation of novel pseudopeptide bradykinin receptor antagonists
Kyle, Donald James; Mavunkel, Babu Joseph
Scios Novel Inc., USA
PCT Int. Appl., 66 pp.
CODEN: PIXXD2
Patent
English
CMT 7
DT Patel.
LA English
FAN.CNT 7
FAN.CNT 7
PI WO 9408607
W: CA. JP
TW: AT. BE,
                                                                                KIND
                                                                                                DATE
                                                                                                                                       APPLICATION NO.
                                                                                                                                                                                                           DATE
                                                                                  A1
                                                                                                   19940428
                                                                                                                                      WO 1993-US9130
                                                                                                                                                                                                           19930927
     PI WO 9408607 A1 19940428 WO 1993-US9130 19930927

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, HC, NL, FT, SE

US 5521158 A 19960528 US 1992-957879 19921008

US 1992-957879 A 19971031 US 1995-416524 19950403

PRAI US 1992-957879 B1 19930909

US 1993-118558 B1 19930909
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The substitution of at least one of the amino acids in positions 2 to 5 of the bradykinin peptide with a fatty acid amide converts bradykinin agonists into bradykinin antagonists. The invention further includes the intermediate compds. and addnl. modifications at other positions within the modified bradykinin antagonists which increase enzyme resistance, antagonist potency and/or specificity of the new bradykinin antagonists. This bradykinin-type peptides are represented by the formula RI-A-B-C-D-E-E-F-G-H-I-J-Cn [RI = hydrogen; A, B = D- or L-Arg, -Gln, -Asn, -Lys, or -Lys(Ac), Arg (Tos), Arg (No2), Lys-Lys, Ac-D-Arg, L-citrulline; C, D = direct bond, Pro, dehydro-Pro, 4-hydroxy-Pro (4Hyp), tetrahydroisoquinoline-3-carboxylic acid (Tic), (S, S, S)-2-azabicyclo(3.3.0) cottane-3-carboxylic acid (Aco), L-azetidine-2-carboxylic acid, e-aminocaproic acid (Eac), Gly, theisolidine 4-carboxylic acid (Thi), (2S, 3aS, 7aS)-octahydro-IH-indole-2-carboxylic acid (Gl), 2-aminoisobutyric acid (Alb), NM(CH2)xCO, Q (wherein x = 2-18), E = direct bond, Gly, Ala, Thr, Ser, NH(CH2)xCO, Q (wherein x = 2-18), F = direct bond, Pie, B-2-thienylalanine (Thi), Leu, Ile, Tic, Oic, bomo-Phe, phenyl-Gly, β-cyclohenylalanine, Val, P-naphthyl-Ala (Nal), Val, NH(CH2)xCO, Q (wherein x = 2-18), G = Ser, Thr. (Hyp, Gly, Val, Ala; H = D-Tic, D-Phe, trans-D-Ql (wherein R = alkyl, alkenyl, aryl, aralkyl etc., X = S, O); I = Phe, Tic, homo-Pro, cis-or trans-L-Ql, etc.; J = Arg, Lys, Orn, Asn, Gln, Lys(Ac), Orn(Ac), Cn = OR, amide, alkoxy, D- or L-amino acid residue, peptide residue containing D- or L-amino acids). The analogs produced are useful for treating human or nammalian conditions and diseases in which an excess of bradykinin or

ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
1991:144010 CAPLUS
114:144010 CAPLUS
114:144010 Design and conformational analysis of several highly potent bradykinin receptor antagonists
Fyla, Donald J., Marcin, Jennifer A.; Farmer, Stephen G.; Burch, Ronald M.
Nova Pharm. Corp., Baltimore, HD, 21224, USA
JOURNAL OF HOMER (1991), 34(3), 1230-3
COUDEN: JHCHAR; ISSN: 0022-2623
JOURNAL FROM PROPERTY (1991), 34(3), 1230-3
FOR THE PROPERTY (1991), 34(3), 1230-3

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H-D-Arg-Arg-Pro-Hyp-Gly-Thi-Cys-X1-Cys-R IV

Drawing on the reported spectroscopic data for bradykinin in solution and,

Drawing on the reported spectroscopic data for bradykinin in solution and, particular, the possible significance of β -turn structures at the C-tarninus of bradykinin receptor-active compds., five peptides H-D-Arg-Arg-Pro-Hyp-Gly-Thi-Ser-D-Tic-X-Arg-OH [Thi = L-4-thiasolidinecarboxylic acid, Tic = 1,2.3,4-tetrahydroisoquinoline-3-carboxylic acid, X = L-Tic (1), D-Tic (11), (1R,45,58)-2-azabicyclo[3.3.3]octane-4-carboxylic acid (IIII), and IV (XI = D-Tic-The-Arg, R = OH XI = D-Ph-Phe, R = Arg-OH) were prepared to challenge the hypothesis and probe the geometric and electronic requirements of the bradykinin receptor. Peptides I, II, and III were expected to stabilize the P-turn via conformationally constrained dihedral angles ψ , vyphi., and χ for the animo acids at positions i and i+1 of the β -turn. Subsequent conformational anal. using empirical energy calens. suggested that only peptides I and III should adopt the desired turn, a result verified by the inactivity of peptide II in the binding assay. Both peptides I and III were highly potent bradykinin receptor antagonists. The β -turn was anticipated to exist in peptides IV due to the disulfide bond cyclization bridging the amino acids at the C-terminus. Emergy calens, performed on these peptides suggested a diminished likelihood of a C-terminal type II' β -turn due to the presence of cis amide bonds and like peptide II, were found to have no activity in the bradykinin receptor binding assay. These peptides support the hypothesis that peptide bradykinin receptor antagonists must adopt a β -turn generally at their c-terminus in order to have a high affinity for the receptor as suggested by previous NMR expts. in nonpolar solvent systems.

ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN (Continued) related kinins is produced or injected as by insect bites, particularly for treating local pain and inflammation from burns, wounds, cuts, rashes, other trauma and pathol. conditions (no data). Thus, D-Arg-Arg-Pro-dHyp-Gly-Thi-Ser-D-Phe-Gic-Arg-GH was prepd. by the solid phase method using a peptide synthesizer (model 9,600, Hilligen Biosearch) Boc-Arg (Tos)-PAM resin and N-Boc-protected amino acids including Boc-Oic-GH, Boc-Thi-GH, and Boc-4Hyp(Bz1)-OH.